AMENDMENT AND RESPONSE UNDER 37 CFR § 1.111

Serial Number: 10/690,798 Filing Date: October 21, 2003

Title: ENHANCED BIOLOGICALLY BASED CHRONOTROPIC BIOSENSING

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IN THE CLAIMS

Please amend the claims as follows:

Claims 1-58 (Cancelled)

- 59. (Withdrawn) An implantable physiological or pathophysiological biosensor comprising: tissue or cells grown on a chip, wherein the tissue or cells are capable of carrying out a physiological or pathophysiological function, wherein the tissue or cells can be coupled via an electrical interface to an electronic measuring device or an electronic amplifying device, and wherein the biosensor monitors a chemical, physiological or pathophysiological variable associated with an endogenous physiological or pathophysiological function in a mammalian subject.
- 60. (Withdrawn) The biosensor according to claim 59, wherein the tissue or cells are coupled via an electrical interface to an electronic measuring device or an electronic amplifying device through the chip.
- 61. (Withdrawn) The biosensor according to claim 59, wherein the tissue or cells are cardiac tissue or cardiac cells.
- 62. (Withdrawn) The biosensor according to claim 59, wherein the tissue or cells are neuronal tissue or neuronal cells.
- 63. (Withdrawn) The biosensor according to claim 59, wherein the tissue or cells are molecularly, genetically, or cellularly engineered.
- 64. (Withdrawn) The biosensor according to claim 63, wherein the tissue or cells are molecularly, genetically, or cellularly engineered to produce a coagulation factor, serotonin, a growth factor, a hormone, or a receptor.

- 65. (Withdrawn) The biosensor according to claim 64, wherein the growth factor is platelet derived growth factor or vascular endothelial growth factor.
- 66. (Withdrawn) The biosensor according to claim 59, wherein the physiological or pathophysiological variable is heart rate regulation or heart rate dynamics.
- 67. (Withdrawn) The biosensor according to claim 59, wherein the physiological or pathophysiological variable is a level or activity of at least one of blood glucose, insulin, thyroid hormone, clotting factors or components, endocrine hormone, paracrine hormone, autocrine hormone, antibodies, receptor antagonists, ligands, antigens, antagonists, signal pathway cofactors, signal pathway components, pathogens, drugs, metabolites, or toxins.
- 68. (Withdrawn) The biosensor according to claim 59, wherein the biosensor is implanted or inserted in an animal.
- 69. (Withdrawn) The biosensor according to claim 68, wherein the animal is a mammal.
- 70. (Withdrawn) The biosensor according to claim 69, wherein the mammal is selected from the group consisting of a mouse, rat, rabbit, pig, cat, dog, cattle, horse, and sheep.
- 71. (Withdrawn) The biosensor according to claim 69, wherein the mammal is a human.
- 72. (Withdrawn) The biosensor according to claim 59, wherein the chip with the tissue or cells are incorporated within a device.
- 73. (Withdrawn) The biosensor of claim 72, wherein the device is at least one of a tube, tubing, catheter, wire, wire leads, or an electronic pacemaker.

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- 74. (Previously Presented) An implantable physiological or pathophysiological biosensor comprising: in vitro or ex vivo modified stem cells coupled to an electrical interface and adapted to be electrically coupled to endogenous tissue or cells when implanted into a mammalian subject at a site distant from a natural site for a physiological or pathophysiological function of the subject, wherein the in vitro or ex vivo modified stem cells can monitor a chemical, physiological or pathophysiological variable associated with the physiological or pathophysiological function of the subject and can produce a coagulation factor, serotonin, a growth factor, a hormone, or a receptor.
- 75. (Previously Presented) The biosensor according to claim 74, wherein the growth factor is platelet derived growth factor or vascular endothelial growth factor.
- 76. (Previously Presented) The biosensor according to claim 74, wherein in vitro or ex vivo modified stem cells are molecularly, genetically, or cellularly engineered.
- 77. (Withdrawn) The biosensor according to claim 74, wherein the physiological or pathophysiological variable is heart rate regulation or heart rate dynamics.
- 78. (Previously Presented) The biosensor according to claim 74, wherein the physiological or pathophysiological variable is a level or activity of at least one of blood glucose, insulin, thyroid hormone, clotting factors or components, endocrine hormone, paracrine hormone, autocrine hormone, antibodies, receptor antagonists, ligands, antigens, antagonists, signal pathway cofactors, signal pathway components, pathogens, drugs, metabolites, or toxins.
- 79. (Cancelled)
- 80. (Cancelled)
- 81. (Currently Amended) The biosensor according to claim <u>74</u> [[80]], wherein the <u>mammalian subject mammal</u> is selected from the group consisting of a mouse, rat, rabbit, pig,

cat, dog, cattle, horse, and sheep.

82. (Currently Amended) The biosensor according to claim 74 [[80]], wherein the mammalian subject mammal is a human.

83. (Previously Presented) The biosensor according to claim 74, wherein the in vitro or ex

vivo modified stem cells are incorporated within a device.

84. (Previously Presented) The biosensor of claim 83, wherein the device is at least one of a

tube, tubing, catheter, wire, wire leads, or an electronic pacemaker.

85. (Withdrawn) An implantable biologically-based biosensor comprising: tissue or cell

contents on a chip, wherein the tissue or cell contents are capable of carrying out a physiological

or pathophysiological function, wherein the tissue or cell contents can be coupled via an

electrical interface to an electronic measuring device or an electronic amplifying device, and

wherein the biosensor monitors a chemical, physiological or pathophysiological variable

associated with an endogenous physiological or pathophysiological function in a mammalian

subject.

86. (Withdrawn) The biosensor according to claim 85, wherein the tissue or cell contents are

coupled via an electrical interface to an electronic measuring device or an electronic amplifying

device through the chip.

87. (Withdrawn) The biosensor according to claim 85, wherein the tissue or cell contents are

cardiac tissue contents or cardiac cell contents.

88. (Withdrawn) The biosensor according to claim 85, wherein the tissue or cell contents are

neuronal tissue contents or neuronal cell contents.

89. (Withdrawn) The biosensor according to claim 85, wherein the biosensor is implanted or

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inserted in an animal.

90. (Withdrawn) The biosensor according to claim 89, wherein the animal is a mammal.

91. (Withdrawn) The biosensor according to claim 90, wherein the mammal is selected from

the group consisting of a mouse, rat, rabbit, pig, cat, dog, cattle, horse, and sheep.

92. (Withdrawn) The biosensor according to claim 90, wherein the mammal is a human.

93. (Withdrawn) The biosensor according to claim 85, wherein the chip with the tissue or

cell contents is incorporated within a device.

94. (Withdrawn) The biosensor of claim 93, wherein the device is at least one of a tube,

tubing, catheter, wire, wire leads, or an electronic pacemaker.

95. (Withdrawn) A method of regulating output of a signal, substance, or action in a subject,

said method comprising: placing within the subject, exogenous tissue or cells capable of carrying

out a physiological or pathophysiological function, wherein the exogenous tissue or cells can be

used to monitor a chemical, physiological or pathophysiological variable associated with the

physiological or pathophysiological function, and wherein the exogenous tissue or cells can

produce a coagulation factor, serotonin, a growth factor, a hormone, or a receptor.

96. (Withdrawn) The method according to claim 95, wherein the growth factor is platelet

derived growth factor or vascular endothelial growth factor.

97. (Withdrawn) The method according to claim 95, wherein the tissue or cells are excitable

tissue or cells.

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98. (Withdrawn) The method according to claim 97, wherein the excitable tissue or cells are cardiac tissue or cells.

- 99. (Withdrawn) The method according to claim 97, wherein the excitable tissue or cells are neuronal tissue or cells.
- 100. (Withdrawn) The method according to claim 95, wherein the tissue or cells are molecularly, genetically, or cellularly engineered.
- 101. (Withdrawn) The method according to claim 95, wherein the physiological or pathophysiological variable is heart rate regulation or heart rate dynamics.
- 102. (Withdrawn) The method according to claim 95, wherein the chemical, physiological or pathophysiological variable is a level or activity of at least one of blood glucose, insulin, thyroid hormone, clotting factors and components, endocrine hormone, paracrine hormone, autocrine hormone, antibodies, receptor antagonists, ligands, antigens, antagonists, signal pathway cofactors, signal pathway components, pathogens, drugs, metabolites or toxins.
- 103. (Withdrawn) The method according to claim 95, wherein the tissue or cells are incorporated into a device that is placed inside the subject.
- 104. (Withdrawn) The method of claim 103, wherein the device is at least one of a tube, tubing, catheter, wire, wire leads, or an electronic pacemaker.
- 105. (Withdrawn) The method according to claim 95, wherein the subject is a mammal selected from the group consisting of a mouse, rat, rabbit, pig, cat, dog, cattle, horse, and sheep.
- 106. (Withdrawn) The method according to claim 105, wherein the mammal is a human.

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(New) The biosensor according to claim 74, further comprising platelet derived growth 107. factor.